Claims

1. A method for producing a xenogeneic immunoglobulin or analog thereof in a non-human animal host, said method comprising:

immunizing said host with an immunogen under conditions to stimulate an immune response to said immunogen, whereby said host mounts an immune response to said immunogen and produces B-cells producing immunoglobulin specific for said immunogen, and isolating xenogeneic immunoglobulin produced by said host,

wherein said host is characterized by 1) being substantially incapable of producing endogenous immunoglobulin heavy chain; 2) being substantially incapable of producing endogenous immunoglobulin light chains; and 3) being capable of producing a xenogeneic immunoglobulin or analog thereof.

2. An immortalized non-human cell line genetically modified so as to lack the ability to produce immunoglobulin endogenous to the cell line and comprising xenogeneic immunoglobulin loci encoding at least one xenogeneic immunoglobulin heavy chain and a light chain;

wherein said xenogeneic immunoglobulin heavy and light chain loci are expressed.

3. A method to produce a xenogeneic immunoglobulin which method comprises culturing the cells of claim 2 under conditions for producing said immunoglobulin and recovering the immunoglobulin produced.

4. A xenogeneic immunoglobulin produced by the method of claim 1 or 3.

5. The immunoglobulin of claim 4 which is a human immunoglobulin.

6. The immunoglobulin of claim 4 which is immunospecific for a human antigen.

7. The immunoglobulin of claim 4 which is immunospecific for an antigen selected from the group consisting of antigens associated with tumors include lymphoma CD19, CD20, CD22, CD56, gangliacide CD3, gangliacide GM2, LMP1, LMP2, HER-2, the Lewis Y antigens, SLe^x, GRP, α7 integrin, L, E, P Lam-1, TNF-α, IL-8 (NAP-1), MIP-1α, MCP-1, MCP-3, RANTES, eosinophil major basic protein, eosinophil cationic protein, high and low affinity IgE Fc receptors (FcϵRI and FcϵRII), gp 39, CD40L, CD40, CD5, CD5a, CD11a, CD11b, CD11c, CD14, CD18, IL-2, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-11, complement receptor 1 (CR1), ICAM-R, ICAM-1, TSST-1, staphylococcal enterotoxin, VLA-4 (α4β1), LPAM-1 (α4β7), VCAM-1, CD4, CD29 (β1), CD27 and ligand, CD30 and ligand, Fas (APO-1) and ligand, TNF receptors, Mac-1 (CD11b/CD18), cutaneous lymphocyte antigen (CLA), gp39, ICAM-1, VLA-4 (α4β1), β7 integrin, gamma interferon, β3 integrin, CD7, L-selectin, Vβ6, Vβ14, Vβ2, MAdCAM-1, IL-12, heat stable antigen, CLA, human IgE, L-selectin, house dust mite antigen, lol p1 (grass allergen), urushiol, CMV glycoprotein B, CMV glycoprotein H, CMV glycoprotein complex II (gCII), HIV-1 envelope glycoprotein, RSV, HSV, EBV, VZV, HPV, CD21, Hepatitis B surface antigen, CD13, ICAM-2, ICAM-3, CD26, gpIIb/IIIa, fibrin, myosin, PDGF receptor, CD4, CD7, CD8 (α and β), CD28, CTLA-4, T cell receptor (TCR/CD3 complex), (CD40 ligand), IL-2 receptor, LFA-1 (CD11a/CD18), CD18, CD2, CD69, B7, B7-2 (B70), B7.3, CD45, LFA-3 and (CD58), TGF-β, various snake venum antigens, and Rh factor.

8. A method for producing a modified non-human animal, said animal having a xenogeneic DNA segment of at least 100 kb stably integrated into the genome of said animal, said method comprising:

combining under fusing conditions yeast spheroplasts, said spheroplasts comprising a YAC having said xenogeneic DNA segment and a marker for selection, with embryonic stem cells of said animal, whereby said xenogeneic DNA segment becomes integrated into the genome of said embryonic stem cells;

selecting for embryonic stem cells carrying said xenogeneic DNA segment by means of the marker;

transferring said embryonic cells into a host blastocyst and implanting said blastocyst in a pseudopregnant animal recipient, and allowing said blastocyst to develop to term to produce a chimeric animal carrying said xenogeneic DNA segment; and

mating said chimeric animal with an animal of the same species to produce said modified animal carrying said xenogeneic DNA segment.

9. An embryonic stem cell comprising a genome having endogenous immunoglobulin heavy chain loci, and immunoglobulin light chain loci, said genome comprising a lesion in said endogenous immunoglobulin heavy chain and/or light loci, resulting in the incapacity of the immunoglobulin locus comprising said lesion to rearrange.

10. A human antibody molecule characterized by

comprising the protein sequences of the human immunoglobulin heavy and light chains;

specificity for an immunogen; and

having other than human glycosylation.

11. A human antibody molecule according to claim 10, wherein said antibody is monoclonal.

12. The antibody molecule according to claim 10 which is immunospecific for an antigen selected from the group consisting of antigens associated with tumors include

lymphoma CD19, CD20, CD22, CD56, gangliacide CD3, gangliacide GM2, LMP1, LMP2, HER-2, the Lewis Y antigens, SLe^x, GRP, α7 integrin, L, E, P Lam-1, TNF-α, IL-8 (NAP-1), MIP-1α, MCP-1, MCP-3, RANTES, eosinophil major basic protein, eosinophil cationic protein, high and low affinity IgE Fc receptors (FcϵRI and FcϵRII), gp 39, CD40L, CD40, CD5, CD5a, CD11a, CD11b, CD11c, CD14, CD18, IL-2, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-11, complement receptor 1 (CR1), ICAM-R, ICAM-1, TSST-1, staphylococcal enterotoxin, VLA-4 (α4β1), LPAM-1 (α4β7), VCAM-1, CD4, CD29 (β1), CD27 and ligand, CD30 and ligand, Fas (APO-1) and ligand, TNF receptors, Mac-1 (CD11b/CD18), cutaneous lymphocyte antigen (CLA), gp39, ICAM-1, VLA-4 (α4β1), β7 integrin, gamma interferon, β3 integrin, CD7, L-selectin, Vβ6, Vβ14, Vβ2, MAdCAM-1, IL-12, heat stable antigen, CLA, human IgE, L-selectin, house dust mite antigen, lol p1 (grass allergen), urushiol, CMV glycoprotein B, CMV glycoprotein H, CMV glycoprotein complex II (gCII), HIV-1 envelope glycoprotein, RSV, HSV, EBV, VZV, HPV, CD21, Hepatitis B surface antigen, CD13, ICAM-2, ICAM-3, CD26, gpIIb/IIIa, fibrin, myosin, PDGF receptor, CD4, CD7, CD8 (α and β), CD28, CTLA-4, T cell receptor (TCR/CD3 complex), (CD40 ligand), IL-2 receptor, LFA-1 (CD11a/CD18), CD18, CD2, CD69, B7, B7-2 (B70), B7.3, CD45, LFA-3 and (CD58), TGF-β, various snake venum antigens, and Rh factor.